General

Guideline Title

Non-Hodgkin's lymphoma: diagnosis and management.

Bibliographic Source(s)

National Collaborating Centre for Cancer. Non-Hodgkin's lymphoma: diagnosis and management. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jul 20. 25 p. (NICE guideline; no. 52).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation) and is defined at the end of the "Major Recommendations" field.

Diagnosis

Type of Biopsy

Consider an excision biopsy as the first diagnostic procedure for people with suspected non-Hodgkin's lymphoma at first presentation.

In people with suspected non-Hodgkin's lymphoma for whom the risk of a surgical procedure outweighs the potential benefits of an excision biopsy, consider a needle core biopsy procedure. Take the maximum number of cores of the largest possible calibre.

For people with suspected non-Hodgkin's lymphoma in whom a diagnosis is not possible after a needle core biopsy procedure, offer an excision biopsy (if surgically feasible) in preference to a second needle core biopsy procedure.

Pathology departments should ensure that tissue is conserved when handling needle core biopsies, so that further analysis can be carried out if needed.

Diagnosing B-cell Lymphomas: Gene Testing Strategies

Consider using FISH (fluorescence in situ hybridisation) to identify a *MYC* rearrangement in all people newly presenting with histologically high-grade B-cell lymphoma.

If a *MYC* rearrangement is found, use FISH to identify the immunoglobulin partner and the presence of *BCL2* and *BCL6* rearrangements.

Stratifying High-grade B-cell Lymphomas Using Laboratory Techniques

Do not use immunohistochemistry to assess the prognostic value associated with cell of origin in people with diffuse large B-cell lymphoma.

Interpret FISH results (*MYC*, *BCL2* and *BCL6* rearrangements) in the context of other prognostic factors (particularly the person's age and International Prognostic Index [IPI]).

Explain FISH results and their potential prognostic value to people with B-cell lymphoma.

Staging Using Fluorodeoxyglucose-Positron Emission Tomography-Computed Tomography (FDG-PET-CT)

Confirming Staging

Offer FDG-PET-CT imaging to confirm staging for people diagnosed with:

- Stage I diffuse large B-cell lymphoma by clinical and CT criteria
- Stage I or localised stage II follicular lymphoma if disease is thought to be encompassable within a radiotherapy field
- Stage I or II Burkitt lymphoma with other low-risk features

For people diagnosed with other subtypes or stages of non-Hodgkin's lymphoma not listed in the recommendation above, consider FDG-PET-CT imaging to confirm staging if the results will alter management.

Assessing Response to Treatment for Diffuse Large B-cell Lymphoma

Do not routinely offer FDG-PET-CT imaging for interim assessment during treatment for diffuse large B-cell lymphoma.

End-of-Treatment Assessment

Offer FDG-PET-CT imaging to assess response at completion of planned treatment for people with:

- Diffuse large B-cell lymphoma
- Burkitt lymphoma

For people with other subtypes of non-Hodgkin's lymphoma not listed in the recommendation above, do not routinely offer FDG-PET-CT imaging to assess response at completion of planned treatment unless the results will alter management.

Consider FDG-PET-CT imaging to assess response to treatment before autologous stem cell transplantation for people with high-grade non-Hodgkin's lymphoma.

Management of Follicular Lymphoma

First-line Treatment for Stage IIA Follicular Lymphoma

Offer local radiotherapy as first-line treatment to people with localised stage IIA follicular lymphoma.

Consider 'watch and wait' (observation without therapy) as first-line treatment for people with stage IIA follicular lymphoma who are asymptomatic and for whom treatment with a single radiotherapy volume is not suitable.

Offer the same treatments that might be offered to people with advanced-stage (stages III and IV) symptomatic follicular lymphoma to people with stage IIA follicular lymphoma who are symptomatic and for whom radiotherapy is not suitable.

Treating Advanced-Stage Asymptomatic Follicular Lymphoma

Offer rituximab induction therapy[1] to people with advanced-stage (stages III and IV) follicular lymphoma who are asymptomatic.

Treating Advanced-stage Symptomatic Follicular Lymphoma

Rituximab, in combination with:

- Cyclophosphamide, vincristine and prednisolone (CVP)
- Cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP)
- Mitoxantrone, chlorambucil and prednisolone (MCP)
- Cyclophosphamide, doxorubicin, etoposide, prednisolone and interferon-α (CHVPi) or
- Chlorambucil
  is recommended as an option for the treatment of symptomatic stage III and IV follicular lymphoma in previously untreated people. (This recommendation is from 'Rituximab for the first-line treatment of stage III–IV follicular lymphoma ' [NICE technology appraisal guidance 243]).

Rituximab maintenance therapy is recommended as an option for the treatment of people with follicular non-Hodgkin's lymphoma that has responded to first-line induction therapy with rituximab in combination with chemotherapy. (This recommendation is from 'Rituximab for the first-line maintenance treatment of follicular non-Hodgkin's lymphoma ' [NICE technology appraisal guidance 226]).

The Guideline Committee did not assess evidence or develop recommendations on bendamustine for treating people with follicular lymphoma, because a NICE technology appraisal on the clinical and cost effectiveness of bendamustine in combination with rituximab within its licensed indication for the first-line treatment of advanced indolent non-Hodgkin's lymphoma was in development. This technology appraisal is currently suspended.

Treating Advanced-Stage Relapsed or Refractory Follicular Lymphoma

The recommendations in this section are from 'Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma ' [NICE technology appraisal guidance 137]).

Rituximab, within its marketing authorisation, in combination with chemotherapy, is recommended as an option for the induction of remission in people with relapsed stage III or IV follicular non-Hodgkin's lymphoma.

Rituximab monotherapy as maintenance therapy, within its marketing authorisation, is recommended as an option for the treatment of people with relapsed stage III or IV follicular non-Hodgkin's lymphoma in remission induced with chemotherapy with or without rituximab.

Rituximab monotherapy, within its marketing authorisation, is recommended as an option for the treatment of people with relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma, when all alternative treatment options have been exhausted (that is, if there is resistance to or intolerance of chemotherapy).

Consolidation with Stem Cell Transplantation

Offer consolidation with autologous stem cell transplantation for people with follicular lymphoma in second or subsequent remission (complete or partial) who have not already had a transplant and who are fit enough for transplantation.

Consider consolidation with allogeneic stem cell transplantation for people with follicular lymphoma in second or subsequent remission (complete or partial):

- Who are fit enough for transplantation and
- For whom a suitable donor can be found and
- When autologous stem cell transplantation has not resulted in remission or is inappropriate (for example, because stem cell harvesting is not possible)

Treating Transformed Follicular Lymphoma

Consider consolidation with autologous stem cell transplantation for people with transformation of previously diagnosed follicular lymphoma that has responded to treatment and who are fit enough for transplantation.

Consider consolidation with autologous or allogeneic stem cell transplantation for people with transformation of follicular lymphoma who need more than 1 line of treatment for a response and who are fit enough for transplantation.

Do not offer consolidation with high-dose therapy and autologous or allogeneic stem cell transplantation to people presenting with concurrent diagnoses of follicular lymphoma and diffuse large B-cell lymphoma that have responded to first-line treatment.

Management of Mucosal-Associated Lymphoid Tissue (MALT) Lymphoma

First-line Treatment

Gastric MALT Lymphoma: Localised Disease

Offer 1 or more lines of *Helicobacter pylori* eradication therapy, without any concurrent therapy, to people with *H. pylori*-positive gastric MALT lymphoma (see the NGC summary of the NICE guideline Dyspepsia and gastro-oesophageal reflux disease in adults. Investigation and management of dyspepsia, symptoms suggestive of gastro-oesophageal reflux disease, or both).

Consider *H. pylori* eradication therapy for people with *H. pylori*-negative gastric MALT lymphoma (see the NGC summary of the NICE guideline Dyspepsia and gastro-oesophageal reflux disease in adults. Investigation and management of dyspepsia, symptoms suggestive of gastro-oesophageal reflux disease, or both).

Consider 'watch and wait' (observation without therapy) for people with gastric MALT lymphoma that responds clinically and endoscopically to *H. pylori* eradication therapy but who have residual disease shown by surveillance biopsies of the stomach, unless high-risk features are present.

For people with residual MALT lymphoma after *H. pylori* eradication therapy who are at high risk of progression [*H. pylori*-negative at initial presentation or t(11:18) translocation], consider a choice of the following, in discussion with the person:

- Chemotherapy (for example, chlorambucil or CVP) in combination with rituximab[2] or
- Gastric radiotherapy

For people with progressive gastric MALT lymphoma, offer a choice of:

- Chemotherapy (for example, chlorambucil or CVP) in combination with rituximab[2] or
- Gastric radiotherapy

Gastric MALT Lymphoma: Disseminated Disease

Offer *H. pylori* eradication therapy to people with disseminated *H. pylori*-positive gastric MALT lymphoma (see the NGC summary of the NICE guideline Dyspepsia and gastro-oesophageal reflux disease in adults. Investigation and management of dyspepsia, symptoms suggestive of gastro-oesophageal reflux disease, or both).

Offer chemotherapy (for example, chlorambucil or CVP) in combination with rituximab[2] to people with disseminated gastric MALT lymphoma who need treatment; for example, people who are symptomatic or with threatened vital organ function.

Consider 'watch and wait' (observation without therapy) for people with disseminated gastric MALT lymphoma who are asymptomatic and do not have threatened vital organ function.

Non-gastric MALT Lymphoma

For people with non-gastric MALT lymphoma, take into account the following before recommending any treatment:

- Site of involvement and potential for organ dysfunction
- Whether it is localised or disseminated
- The morbidity associated with any treatment proposed
- The person's overall fitness

Offer chemotherapy (for example, chlorambucil or CVP) in combination with rituximab[2] to people with non-gastric MALT lymphoma for whom radiotherapy is not suitable or who have disseminated disease and need treatment.

Consider radiotherapy for people with localised disease sites of non-gastric MALT lymphoma, irrespective of stage.

Consider 'watch and wait' (observation without therapy) for people with clinically non-progressive localised non-gastric MALT lymphoma that is unlikely to result in vital organ dysfunction, who are asymptomatic and for whom radiotherapy is not suitable.

Management of Mantle Cell Lymphoma

First-line Treatment

Offer chemotherapy in combination with rituximab[2] as first-line treatment for people with advanced-stage mantle cell lymphoma who are symptomatic. Take the person's fitness into account when deciding on the intensity of chemotherapy.

Consider cytarabine[3]-containing immunochemotherapy for people with advanced-stage mantle cell lymphoma who are fit enough to tolerate an intensive approach.

Consider radiotherapy for people with localised stage I or II mantle cell lymphoma.

Consider 'watch and wait' (observation without therapy) until disease progression for people with clinically non-progressive mantle cell lymphoma who are asymptomatic and for whom radiotherapy is not suitable.

Bortezomib is recommended, within its marketing authorisation, as an option for previously untreated mantle cell lymphoma in adults for whom haematopoietic stem cell transplantation is unsuitable. (This recommendation is from 'Bortezomib for previously untreated mantle cell lymphoma ' [NICE technology appraisal guidance 370).]

The guideline committee did not assess evidence or develop recommendations on bendamustine for treating people with mantle cell lymphoma, because a NICE technology appraisal on the clinical and cost effectiveness of bendamustine in combination with rituximab within its licensed indication for the first-line treatment of mantle cell lymphoma was in development. This technology appraisal is currently suspended.

Consolidation with Stem Cell Transplantation

Consider consolidation with autologous stem cell transplantation for people with chemosensitive mantle cell lymphoma (that is, there has been at least a partial response to induction chemotherapy) who are fit enough for transplantation.

Maintenance Strategies

Consider maintenance rituximab[4], every 2 months until disease progression, for people with newly diagnosed mantle cell lymphoma who are not fit enough for high-dose chemotherapy and where there has been a response to rituximab-cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP)-based immunochemotherapy.

Consider maintenance rituximab[5], every 2 months for 3 years, for people with newly diagnosed mantle cell lymphoma who are in remission after cytarabine-based induction and high-dose chemotherapy.

Management of Diffuse Large B-cell Lymphoma

Radiotherapy in First-line Treatment

Consider consolidation radiotherapy delivering 30 Gy to sites involved with bulk disease at diagnosis for people with advanced-stage diffuse large B-cell lymphoma that has responded to first-line immunochemotherapy. For each person, balance the possible late effects of radiotherapy with the possible increased need for salvage therapy if it is omitted, and discuss the options with them.

Central Nervous System Prophylaxis

Explain to people with diffuse large B-cell lymphoma that they have an increased risk of central nervous system lymphoma if the testis, breast, adrenal gland or kidney is affected.

Explain to people with diffuse large B-cell lymphoma that they may have an increased risk of central nervous system lymphoma if they have 2 or more of the following factors:

- Elevated lactate dehydrogenase (LDH)
- Age over 60 years
- Poor performance status (Eastern Cooperative Oncology Group [ECOG] score of 2 or more)
- More than one extranodal site involved
- Stage III or IV disease
  Explain that the level of risk increases with the number of factors involved.

Offer central nervous system-directed prophylactic therapy to people with diffuse large B-cell lymphoma:

- That involves the testis, breast, adrenal gland or kidney or
- Who have 4 or 5 of the factors associated with increased risk of central nervous system relapse listed in the recommendation above
  Consider central nervous system-directed prophylactic therapy for people with diffuse large B-cell lymphoma who have 2 or 3 of the factors associated with increased risk of central nervous system relapse listed in the recommendation above.

Salvage Therapy and Consolidation with Stem Cell Transplantation

Offer salvage therapy with multi-agent immunochemotherapy to people with relapsed or refractory diffuse large B-cell lymphoma who are fit enough to tolerate intensive therapy:

- Explain that this is primarily to obtain sufficient response to allow consolidation with autologous or allogeneic stem cell transplantation, but is also beneficial even if not followed by transplantation
- Consider rituximab, gemcitabine dexamethasone and cisplatin (R-GDP) immunochemotherapy, which is as effective as other commonly used salvage regimens and less toxic.

Offer consolidation with autologous stem cell transplantation to people with chemosensitive diffuse large B-cell lymphoma (that is, there has been at least a partial response to chemotherapy) who are fit enough for transplantation.

Consider consolidation with allogeneic stem cell transplantation for people with chemosensitive diffuse large B-cell lymphoma (that is, there has been at least a partial response to chemotherapy):

- That relapses after autologous stem cell transplantation or
- In whom stem cell harvesting is not possible

Management of Burkitt Lymphoma

First-line Treatment

Offer intensive immunochemotherapy to people with Burkitt lymphoma who are fit enough to tolerate it. Consider using one of the following:

- Rituximab plus Berlin-Frankfurt-Munster regimen (R-BFM)
- Rituximab, cyclophosphamide, doxorubicin, vincristine, cytarabine and methotrexate (R-CODOX-M)/rituximab, ifosfamide, etoposide, high-dose cytarabine (R-IVAC)
- Rituximab, cyclophosphamide, vincristine, doxorubicin and dexamethasone, (methotrexate and cytarabine) (R-HyperCVAD [HDMTX])
- Rituximab plus Lymphome Malin B regimen (R-LMB)

For people with low-risk Burkitt lymphoma, consider using the less intensive rituximab, etoposide, prednisolone, vincristine, cyclophosphamide and doxorubicin (DA-EPOCH-R) regimen supplemented with intravenous and/or intrathecal methotrexate.

Offer less intensive immunochemotherapy to people with Burkitt lymphoma who are not fit enough to tolerate intensive chemotherapy. Consider using one of the following, alone or supplemented with intravenous and/or intrathecal methotrexate:

- R-CHOP
- Rituximab, cyclophosphamide, doxorubicin, etoposide, vincristine and prednisolone (R-CHEOPP)
- DA-EPOCH-R

Management of Peripheral T-cell Lymphoma

First-line Treatment

Consider CHOP chemotherapy as first-line treatment for people with peripheral T-cell lymphoma.

Consolidation Therapy

Consider consolidation with autologous stem cell transplantation for people with chemosensitive peripheral T-cell lymphoma (that is, there has been at least a partial response to first-line chemotherapy) who are fit enough for transplantation.

Information and Support

To help people with non-Hodgkin's lymphoma (and their family members or carers as appropriate) to make decisions about care, follow the recommendations in the NICE guidelines on patient experience in adult National Health Service (NHS) services , improving outcomes in haematological cancers – the manual (patient-centred care), and improving supportive and palliative care for adults with cancer , and the NGC summary of the NICE guideline Care of dying adults in the last days of life. Pay particular attention to the following areas:

- Establishing the best way of communicating with the person

- Timing and format of information
- Information about treatment, including benefits, short-term risks and late effects
- Financial support and benefit advice
- Fertility issues
- Sexual function
- Support groups
- Access to wellbeing services and psychological support

Give people with non-Hodgkin's lymphoma (and their family members or carers as appropriate) detailed information about the nature and purpose of diagnostic and staging tests, including:

- Bone marrow biopsies
- Central line insertion
- Core and excision biopsies
- CT and PET-CT scans
- Lumbar punctures

If 'watch and wait' (observation without therapy) is suggested for a person with non-Hodgkin's lymphoma:

- Explain to them (and their family members or carers as appropriate) about what this involves and why it is being advised.
- Address any increased anxiety that results from this approach.

Explain to people with low-grade non-Hodgkin's lymphoma about the possibility of transformation to high-grade lymphoma, taking into account the person's needs and preferences. Involve family members or carers as appropriate.

Ensure that people with non-Hodgkin's lymphoma have:

- A named key worker at diagnosis and during treatment and
- Contact details for the specialist team after treatment

Discuss exercise and lifestyle with people with non-Hodgkin's lymphoma from diagnosis onwards.

Follow-up for People with Diffuse Large B-cell Lymphoma

For people in complete remission after first-line treatment with curative intent for diffuse large B-cell lymphoma:

- Offer regular clinical assessment
- Consider stopping regular clinical assessment aimed at detecting relapse 3 years after completing treatment for people in ongoing complete remission
- Offer urgent appointments to people who experience a recurrence of lymphoma symptoms or new symptoms that suggest disease relapse
- Do not offer LDH surveillance for detecting relapse
- Do not offer routine surveillance imaging (including chest X-ray, CT and PET-CT) for detecting relapse in people who are asymptomatic

Survivorship

Provide end-of-treatment summaries for people with non-Hodgkin's lymphoma (and their general practitioners [GPs]). Discuss these with the person, highlighting personal and general risk factors, including late effects related to their lymphoma subtype and/or its treatment.

Provide information to people with non-Hodgkin's lymphoma when they complete treatment about how to recognise possible relapse and late effects of treatment.

At 3 years after a person with non-Hodgkin's lymphoma completes a course of treatment, consider switching surveillance of late effects of treatment to nurse-led or GP-led services.

Footnotes

[1]At the time of publication (July 2016) rituximab did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information. The evidence reviewed for the guideline supports the standard monotherapy dosage of 4 doses of 375 mg/m^2 at weekly intervals.)

[2]At the time of publication (July 2016) rituximab did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines

for further information.

[3]At the time of publication (July 2016) cytarabine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[4]At the time of publication (July 2016) rituximab did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information. The evidence reviewed for the guideline supports a dosage of 375 mg/m^2 every 2 months until disease progression.

[5]At the time of publication (July 2016) rituximab did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information. The evidence reviewed for the guideline supports a dosage of 375 mg/m^2 every 2 months for 3 years.

Definitions

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Committee (GC) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GC is confident that, given the information it has looked at, most people would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GC usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GC uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of people, an intervention will do more good than harm, and be cost effective. The GC uses similar forms of words (for example, 'Do not offer…') when they are confident that an intervention will not be of benefit for most people.

Interventions That Could Be Used

The GC uses 'consider' when confident that an intervention will do more good than harm for most people, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the person's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the person.

Clinical Algorithm(s)

A National Institute for Health and Care Excellence (NICE) pathway titled "Non-Hodgkin's lymphoma overview" is available on the NICE Web site.

Scope

Disease/Condition(s)

Non-Hodgkin's lymphoma, including:

- Follicular lymphoma
- Mucosal-associated lymphoid tissue (MALT) lymphoma
- Mantle cell lymphoma
- Diffuse large B-cell lymphoma
- Burkitt lymphoma
- Peripheral T-cell lymphoma

Guideline Category

Diagnosis

Evaluation

Management

Risk Assessment

Treatment

Clinical Specialty

Family Practice

Hematology

Internal Medicine

Medical Genetics

Oncology

Radiation Oncology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Patients

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

- To help healthcare professionals and patients make informed choices about appropriate healthcare
- To facilitate standardisation of practice in treating non-Hodgkin's lymphoma
- To improve care for people with non-Hodgkin's lymphoma by promoting the best tests for diagnosis and staging and the most effective treatments for 6 of the subtypes

Target Population

Adults and young people (aged 16 years and over) referred to secondary care with suspected non-Hodgkin's lymphoma or with newly diagnosed or relapsed non-Hodgkin's lymphoma

Interventions and Practices Considered

Diagnosis/Evaluation

1. Biopsy (excision or needle core)
2. Gene testing (fluorescence in situ hybridization [FISH])
3. Stratifying high-grade B-cell lymphomas using laboratory techniques
4. Staging using fluorodeoxyglucose-positron emission tomography-computed tomography (FDG-PET-CT)

Treatment/Management

1. Management of follicular lymphoma
    - First-line treatment for early stage
    - Consolidation therapy
    - Treating advanced-stage asymptomatic follicular lymphoma
    - Treating advanced-stage symptomatic follicular lymphoma
    - Treating advanced-stage relapsed or refractory follicular lymphoma
    - Treating transformed follicular lymphoma
2. Management of mucosa-associated lymphoid tissue (MALT) lymphoma
    - First-line treatment of localised gastric disease
    - First-line treatment of disseminated gastric disease
    - First-line treatment of non-gastric disease
3. Management of mantle cell lymphoma
    - First-line treatment
    - Consolidation therapy
    - Maintenance strategies
4. Management of diffuse large B-cell lymphoma (DLBCL)
    - Radiotherapy in first-line treatment
    - Central nervous system prophylaxis
    - Salvage therapy
5. Management of Burkitt lymphoma
6. Management of peripheral T-cell lymphoma
    - First-line treatment
    - Consolidation therapy
7. Providing for patient information needs (information and support)
8. Follow-up of DLBCL
9. Providing for survivorship (providing end-of-treatment summaries and information on recognition of relapse and late effects of treatment)

Note: Immunohistochemistry was considered but not recommended.

Major Outcomes Considered

- Accuracy of diagnostic test
- Overall survival
- Progression-free survival
- Disease-related morbidity and mortality
- Treatment-related morbidity and mortality
- Health-related quality of life
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

Developing Clinical Evidence-based Questions

Background

The scope for this guideline was very clear about which patient groups were included and which areas of clinical care should be considered (see Appendix E). The 24 review questions and search strategies that covered the guideline topics were agreed during scoping. All the evidence used to inform this guideline is summarised in the accompanying full evidence review 'Non Hodgkin's lymphoma: diagnosis and management – evidence review', which includes details of all the studies appraised (see Appendix G).

Methods

From each of the key clinical issues identified in the scope, the GC formulated a review question. For intervention questions the PICO framework was used. This structured approach divides each question into four components: P – the population (the population under study); I – the intervention(s) (what is being done); C – the comparison (other main treatment or test options); O – the outcomes (the measures of how effective the interventions have been). Diagnostic review questions specified the population, index test, reference standard test and the target condition. Prognostic review questions specified the population, prognostic factors and outcomes.

Review of Clinical Literature

Scoping Search

An initial scoping search for published guidelines, systematic reviews, economic evaluations and ongoing research was carried out on the following databases or Web sites: National Health Service (NHS) Evidence, NICE, Cochrane Databases of Systematic Reviews (CDSR), Health Technology Assessment Database (HTA), Turning Research into Practice (TRIP), Scottish Intercollegiate Guidelines Network (SIGN), NHS Economic Evaluations Database (NHS EED), Health Economic Evaluations Database (HEED), Medline and EMBASE.

At the beginning of the development phase, initial scoping searches were carried out to identify any relevant guidelines/guidance (local, national or international) produced by other groups or institutions which were cross checked for relevant evidence.

Developing the Review Protocol

For each review question, the information specialist and researcher (with input from other technical team and Guideline Committee [GC] members) prepared a review protocol. This protocol explained how the review was to be carried out (see Table 1 in the full version of the guideline) in order to develop a plan of how to review the evidence, limit the introduction of bias and for the purposes of reproducibility. All review protocols can be found in Appendix J.

Searching for the Evidence

In order to answer each question the lead National Collaborating Centre for Cancer (NCC-C) information specialist developed a search strategy to identify relevant published evidence for both clinical and cost-effectiveness. Key words and terms for the search were agreed in collaboration with the GC. When required, the health economist searched for supplementary papers to inform detailed health economic work (see 'Incorporating Health Economic Evidence' below).

Search filters, such as those to identify systematic reviews (SRs) and randomised controlled trials (RCTs), were applied to the search strategies when necessary. No language restrictions were applied to the search; however, foreign language papers were not requested or reviewed (unless of particular importance to that question).

The following databases were included in the literature search:

- The Cochrane Library
- Medline and Premedline 1946 onwards
- Excerpta Medica (EMBASE) 1974 onwards
- Web of Science (specifically Science Citation Index Expanded [SCI-Expanded] 1900 onwards and Social Sciences Citation Index [SSCI] 1900 onwards)

Subject specific databases used for certain topics:

- Cumulative Index to Nursing and Allied Health Literature (CINAHL) 1937 onwards
- PsycINFO 1806 onwards
- Allied and Complementary Medicine (AMED) 1985 onwards

From this list the information specialist sifted and removed any irrelevant material based on the title or abstract before passing to the researcher. All the remaining articles were then stored in a Reference Manager electronic library.

In accordance with the 'NICE guidelines manual' (NICE 2012) (see the "Availability of Companion documents" field) searches were updated and re-run 8 weeks before the guideline was submitted to NICE for stakeholder consultation, thereby ensuring that the latest relevant published evidence was included in the database. Any evidence published after this date was not included. For the purposes of updating this guideline, 1st September 2015 should be considered the starting point for searching for new evidence.

Further details of the search strategies, including the methodological filters used, are provided in Appendix I.

Critical Appraisal

Following the literature search one researcher independently scanned the titles and abstracts of every article for each question, and full publications were obtained for any studies considered relevant or where there was insufficient information from the title and abstract to make a decision. When papers were obtained, the researcher applied the inclusion and exclusion criteria outlined in the review protocol to select appropriate studies.

Incorporating Health Economics Evidence

The aim of providing economic input into the development of the guideline was to inform the GC of potential economic issues relating to the topics identified in the scope. Health economics is about improving the health of the population through the efficient use of resources. In addition to assessing clinical effectiveness, it is important to investigate whether health services are being used in a cost-effective manner in order to maximise health gain from available resources.

Prioritising Topics for Economic Analysis

After the review questions had been defined, and with the help of the health economist, the priority review questions for economic analysis were discussed and agreed. These priorities were chosen on the basis of the following criteria, in broad accordance with the NICE guidelines manual (2012):

- The overall importance of the recommendation, which may be a function of the number of patients affected and the potential impact on costs and health outcomes per patient
- The current extent of uncertainty over cost-effectiveness, and the likelihood that economic analysis will reduce this uncertainty
- The feasibility of building an economic model

A review of the economic literature was conducted at scoping. Where published economic evaluation studies were identified that addressed the economic issues for a review question, these are presented alongside the clinical evidence.

For systematic searches of published economic evidence, the following databases were included:

- Medline
- EMBASE
- NHS EED
- HTA
- HEED

Methods for Reviewing Economic Evidence

The aim of reviewing and appraising the existing economic literature is to identify relevant economic evaluations that compare both costs and health consequences of alternative interventions and that are applicable to NHS practice. Thus studies that only report costs, non-comparative studies of 'cost of illness' studies are generally excluded from the reviews.

Economic studies identified through a systematic search of the literature are appraised using a methodology checklist designed for economic evaluations. This checklist is not intended to judge the quality of a study per se, but to determine whether an existing economic evaluation is useful to inform the decision-making of the GC for a specific topic within the guideline. There are two parts of the appraisal process; the first step is to

assess applicability (i.e., the relevance of the study to the specific guideline topic and the NICE reference case) (see Table 4 in the full version of the guideline).

Number of Source Documents

Clinical Evidence

The number of studies identified for each clinical question is provided in Appendix G in the full guideline appendices (see the "Availability of Companion Documents" field). Study flow diagrams for each question provide the number of records screened, records excluded, records assessed for eligibility, and studies included in the evidence review.

Existing Economic Evidence

A systematic literature review identified one paper that was deemed to be partially applicable to one of the economic topics. A de novo economic model was developed by the Guideline Committee (GC) to estimate the cost-utility of autologous transplantation and allogeneic transplantation compared to no transplantation for people with follicular lymphoma. See Appendices A and B in the full guideline appendices for cost-utility and cost-effectiveness analyses.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

Review of Clinical Literature

Critical Appraisal and Evidence Grading

Each study was critically appraised using a methodology checklist appropriate for its design (Appendices B to I of the 'NICE guidelines manual', NICE 2012 [see the "Availability of Companion Documents" field]): for example the quality of individual diagnostic accuracy studies was assessed

using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool.

When high quality published systematic reviews were identified, the inclusion and exclusion criteria and outcomes were carefully checked against the guideline review protocol and any relevant systematic reviews included as evidence. The risk of bias of the evidence base in the systematic review was estimated using the reported study characteristics. Lists of studies in systematic reviews were checked against any other included studies to avoid double counting.

If results from a study were published as more than one paper, the most recent or complete publication was used. For each question, data were extracted and recorded in evidence tables and an accompanying evidence summary prepared for the Guideline Committee (GC) (see Appendix G). All evidence was considered carefully by the GC for accuracy and completeness.

GRADE (Grading of Recommendations, Assessment, Development and Evaluation)

For interventional questions, studies which matched the inclusion criteria were evaluated and presented using GRADE (http://gradeworkinggroup.org /). Where possible, this included meta-analysis and synthesis of data into a GRADE 'evidence profile'. The evidence profile shows, for each outcome, an overall assessment of both the quality of the evidence as a whole (very low, low, moderate or high) as well as an estimate of the size of effect. A narrative summary of the evidence (evidence statement) was also prepared.

Each outcome was examined for the quality elements defined in Table 2 in the full version of the guideline. The quality levels of evidence are listed in the "Rating Scheme for the Strength of the Recommendations" field.

The reasons for downgrading or upgrading specific outcomes were explained in footnotes and were categorised as due to limitations, inconsistency, indirectness or imprecision. See the Methodology section of the full version of the guideline for information on the reasons for downgrading or upgrading specific outcomes.

Data Synthesis

There were no opportunities for new meta-analyses of randomised trials due to the lack of multiple similar trials in the evidence base (although a published meta-analyses of randomised trials was included as evidence). Formal adjusted indirect comparison of a pair of randomised trials was done using the method suggested by Bucher et al. (1997).

Meta-analysis of diagnostic data was done using the bivariate model of Reitsma et al. (2005) via the R package mada (Doebler, 2015). Any original meta-analysis was accompanied by forest plots or receiver operating characteristic (ROC) plots of confidence regions for sensitivity and specificity.

Data from observational studies were summarised per outcome in GRADE using the range of reported values. For interventions where the only available data came from non comparative observational studies, single arm data were entered into the GRADE evidence profile although relative effect estimates were not estimable.

When data could not be combined (due to differences in study populations, interventions or outcomes) results were summarised and included in GRADE on an individual study basis.

Incorporating Health Economics Evidence

Methods for Reviewing and Appraising Economic Evidence

Economic studies identified through a systematic search of the literature are appraised using a methodology checklist designed for economic evaluations (NICE 2012). This checklist is not intended to judge the quality of a study per se, but to determine whether an existing economic evaluation is useful to inform the decision-making of the GC for a specific topic within the guideline. There are two parts of the appraisal process; the first step is to assess applicability (i.e., the relevance of the study to the specific guideline topic and the NICE reference case) (see Table 4 in the full version of the guideline). In the second step, only those studies deemed directly or partially applicable are further assessed for limitations (i.e., the methodological quality [see Table 5 in the full version of the guideline]).

Where relevant, a summary of the main findings from the systematic search, review and appraisal of economic evidence is presented in an economic evidence profile alongside the clinical evidence.

If high-quality published economic evidence relevant to current National Health Service (NHS) practice was identified through the search, the existing literature was reviewed and appraised. However, it is often the case that published economic studies may not be directly relevant to the specific review question as defined in the guideline or may not be comprehensive or conclusive enough to inform UK practice. In such cases, for priority topics, consideration was given to undertaking a new economic analysis as part of this guideline.

Economic Modelling

Once the need for a new economic analysis for high priority topics had been agreed by the GC, the health economist investigated the feasibility of developing an economic model. In the development of the analysis, the following general principles were adhered to:

- The GC subgroup was consulted during the construction and interpretation of the analysis.
- The analysis was based on the best available clinical evidence from the systematic review.
- Assumptions were reported fully and transparently.
- Uncertainty was explored through sensitivity analysis.
- Costs were calculated from a health services perspective.
- Outcomes were reported in terms of quality-adjusted life years.

See Appendix A and Appendix B for the overview of the de novo economic models.

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

The Guideline Development Process – Who Develops the Guideline?

Overview

The development of this guideline was based upon methods outlined in the 'NICE guidelines manual' (NICE 2012, NICE 2014) (see the "Availability of Companion Documents" field). A team of health professionals, lay representatives and technical experts known as the Guideline Committee (GC), with support from the NCC-C staff, undertook the development of this clinical guideline. The basic steps in the process of developing a guideline are listed and discussed below:

- Defining the scope which sets the inclusion/exclusion criteria of the guideline
- Forming the GC
- Developing review questions
- Identifying the health economic priorities
- Developing the review protocols
- Systematically searching for the evidence
- Critically appraising the evidence
- Incorporating health economic evidence
- Distilling and synthesising the evidence and writing recommendations
- Agreeing the recommendations
- Structuring and writing the guideline
- Consultation and validation

The Scope

The scope was drafted by the GC Chair and Lead Clinician and staff at the NCC-C in accordance with processes established by NICE (NICE 2012). The purpose of the scope was to:

- Set the boundaries of the development work and provide a clear framework to enable work to stay within the priorities agreed by NICE and the NCC-C
- Inform professionals and the public about the expected content of the guideline
- Provide an overview of the population and healthcare settings the guideline would include and exclude

- Specify the key clinical issues that will be covered by the guideline
- Inform the development of the review questions and search strategies

Before the guideline development process started, the draft scope was presented and discussed at a stakeholder workshop. The suggested key clinical issues for inclusion were discussed and revised before the formal consultation process began. Comprehensive details of the discussion at the stakeholder workshop can be found on the NICE Web site (www.nice.org.uk).

The scope was subject to a four week stakeholder consultation in accordance with NICE processes. The full scope is shown in Appendix E. During the consultation period, the scope was posted on the NICE Web site. Comments were invited from registered stakeholder organisations and NICE staff. The NCC-C and NICE reviewed the scope in light of comments received, and the revised scope was reviewed and signed off by NICE and posted on the NICE Web site.

The Guideline Committee (GC)

The non-Hodgkin's lymphoma GC was recruited in line with the 'NICE guidelines manual' (NICE 2012). The first step was to appoint a Chair and a Lead Clinician. Advertisements were placed for both posts and shortlisted candidates were interviewed in person prior to being offered the role. The NCC-C Director, GC Chair and Lead Clinician identified a list of specialties that needed to be represented on the GC. Adverts were sent to all the registered stakeholder organisations including patient organisations/charities (see Appendix F). Individual GC members were selected for interview by the NCC-C Director, GC Chair and Lead Clinician, based on their application forms. The guideline development process was supported by staff from the NCC-C, who undertook the clinical and health economics literature searches, reviewed and presented the evidence to the GC, managed the process and contributed to drafting the guideline.

Guideline Committee Meetings

Fourteen GC meetings were held between 4-5 March 2014 and 4–5 April 2016. During each GC meeting (held over either 1 or 2 days) clinical and health economic evidence were reviewed, assessed and recommendations formulated. At each meeting patient/carer and service-user concerns were routinely discussed, including a standard agenda item.

The NCC-C project manager divided the GC workload by allocating specific review questions, relevant to their area of clinical practice, to small sub-groups of the GC in order to simplify and speed up the development process. These groups considered the evidence, as appraised by the researcher, and synthesised it into draft recommendations before presenting it to the GC. These recommendations were then discussed and agreed by the GC as a whole. Each review question was led by a GC member with expert knowledge of the clinical area (usually one of the healthcare professionals). The GC subgroups often helped refine the review questions and the clinical definitions of treatments. They also assisted the NCC-C team in drafting the section of the guideline relevant to their specific topic.

Patient/Carer Members

Individuals with direct experience of non-Hodgkin's lymphoma services gave an important user focus to the GC and the guideline development process. The GC included three patient/carer members. They contributed as full GC members to writing the review questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology relevant to the guideline and bringing service-user research to the attention of the GC.

Agreeing the Recommendations

For each review question the GC were presented with a summary of the clinical evidence, and, where appropriate, economic evidence, derived from the studies reviewed and appraised. The GC derived their guideline recommendations from this information. The link between the evidence and the view of the GC in making each recommendation was made explicitly in the accompanying linking evidence to recommendations (LETR) statement (see below).

Wording of the Recommendations

The wording used in the recommendations in this guideline denotes the certainty with which the recommendations were made. Some recommendations were made with more certainty than others. Recommendations are based on the trade-off between the benefits and harms of an intervention, whilst taking into account the quality of the underpinning evidence.

For all recommendations, it is expected that a discussion will take place with the patients about the risks and benefits of the interventions, and their values and preferences. This discussion should help the patient reach a fully informed decision. Terms used within this guideline are:

- 'Offer' – for the vast majority of patients, an intervention will do more good than harm (based on high quality evidence)
- 'Do not offer' – the intervention will not be of benefit for most patients (based on high quality evidence)

- 'Consider' – the benefit is less certain, and an intervention will do more good than harm for most patients (based on poor quality evidence or no evidence). The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for an 'offer' recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Any exceptions to the above were documented in the LETR that accompany the recommendations.

LETR Statements

Each recommendation is accompanied by a section describing the decision making process of the GC and how they used the evidence. This is known as the 'LETR statement' and will usually cover the following key points:

- The relative value placed on the outcomes considered
- The strength of evidence about benefits and harms for the intervention being considered
- The costs and cost-effectiveness of an intervention
- The quality of the evidence
- The degree of consensus within the GC
- Other considerations – for example equalities issues

Where evidence was weak or lacking the GC agreed the final recommendations through informal consensus.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Committee (GC) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GC is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GC usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GC uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words are used (for example, 'do not offer…') when the GC is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GC uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

A Cost-Utility Analysis of Autologous and Allogeneic Transplantation for People with Follicular Lymphoma

Summary

The base case results suggest that both autologous stem cell transplantation (ASCT) and allogeneic stem cell transplantation (allo-HSCT) are cost-effective compared to rituximab (R)-chemotherapy with incremental cost-effectiveness ratios (ICERs) of £4,812 and £12,244, respectively. Allo-HSCT is more expensive and less effective compared to ASCT and is therefore dominated. Sensitivity analyses confirm these results. However, allo-HSCT does emerge as the optimal strategy in scenarios where ASCT relapse rates are increased compared to allo-HSCT. This result was

also strengthened in the probabilistic sensitivity analysis where ASCT was found to be the optimal strategy in 94.8% of runs with allo-HSCT being the optimal strategy in the remaining 5.2% of runs. It can therefore be concluded that the economic evaluation provides robust evidence that ASCT is the most cost-effective treatment strategy for people with relapsed follicular lymphoma in second and third line. Furthermore, ASCT is the most cost-effective transplantation strategy at the point of first transplant. However, allo-HSCT can be cost-effective compared to ASCT in cases where ASCT is not expected to be successful.

See Appendix A in the full guideline appendices (see the "Availability of Companion Documents" field) for additional information on this topic.

The Role of Immediate Compared with Deferred Chemotherapy (Watch and Wait) in Treating Advanced Asymptomatic Follicular Lymphoma

This analysis aimed to estimate the cost-effectiveness of management strategies for patients with newly diagnosed asymptomatic advanced (stage II-IV) follicular lymphoma. In particular, whether an active treatment strategy with rituximab should be adopted or a watchful waiting approach.

Conclusion

The results of the base case analysis suggest that rituximab induction alone is the optimal strategy to adopt in patients with asymptomatic follicular lymphoma. This result was shown to be robust in one-way sensitivity analysis, where rituximab induction remained cost-effective in the vast majority of scenarios. The result was further strengthened in probabilistic sensitivity analysis (PSA) where the strategy was found to have a 68% probability of being cost-effective at a threshold of £20,000 per quality-adjusted life year (QALY). Furthermore, rituximab maintenance was shown to have the next highest probability of being cost-effective with a 21% probability of being cost-effective at the £20,000 per QALY threshold, suggesting that there is a strong case for active treatment (i.e., 89% probability of active treatment being cost-effective) rather than a watchful waiting approach.

See Appendix B in the full guideline appendices for additional information on this topic.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Consultation and Validation of the Guideline

The draft of the guideline was prepared by National Collaborating Centre for Cancer (NCC-C) staff in partnership with the Guideline Committee (GC) Chair and Lead Clinician. This was then discussed and agreed with the GC and subsequently forwarded to the National Institute for Health and Care Excellence (NICE) for consultation with stakeholders.

Registered stakeholders (see Appendix F in the full guideline appendices [see the "Availability of Companion Documents" field]) had one opportunity to comment on the draft guideline which was posted on the NICE website between 29 January 2016 and 11 March 2016 in line with NICE methodology (NICE 2014 [see the "Availability of Companion Documents" field]).

The Pre-publication Process

An embargoed pre-publication version of the guideline was released to registered stakeholders who have signed a confidentiality form to allow them to see how their comments have contributed to the development of the guideline and to give them time to prepare for publication (NICE 2014).

The final document was then submitted to NICE for publication on their Web site. The other versions of the guideline were also discussed and approved by the GC and published at the same time.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type and quality of evidence supporting each review question are described in evidence profiles in the full version of the guideline and Appendix G (see the "Availability of Companion Documents" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Practice standardisation in treating non-Hodgkin's lymphoma

See the "Trade-off between clinical benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for details about benefits of specific interventions.

Potential Harms

- Chemotherapy and radiotherapy can cause physical problems long after the treatment has ended. Heart damage, peripheral neuropathy, cognitive disorders, second cancers, infertility, chronic tiredness and inability to do day to day tasks are some of the late side effects that can happen after lymphoma treatment. People can also have long term psychological and emotional late effects following non-Hodgkin's lymphoma (NHL) treatment, such as depression, anxiety and even post-traumatic stress disorder, affecting families and carers too. The quality of life of long term NHL survivors at 10 years after treatment indicates that up to a quarter of patients surveyed have poor or worsening physical and mental health. This suggests that late effects can continue for many years.
- The 2013 national cancer survey, including lymphoma patients, suggested that cancer treatment makes other health problems worse and reduces quality of life.

See the "Trade-off between clinical benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for details about harms of specific interventions.

Qualifying Statements

Qualifying Statements

- The recommendations in this guideline represent the view of the National Institute for Health and Care Excellence (NICE), arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The application of the recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.
- Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.
- This guideline addresses a number of areas where there is uncertainty or variation in clinical practice, in relation to diagnosing non-Hodgkin's lymphoma and management of the subtypes at different times in the course of the disease. It is not intended as a comprehensive guide to diagnosing and treating lymphomas.

Implementation of the Guideline

Description of Implementation Strategy

Putting This Guideline into Practice

The National Institute for Health and Care Excellence (NICE) has produced tools and resources to help put this guideline into practice (see also the "Availability of Companion Documents" field).

Putting recommendations into practice can take time. How long may vary from guideline to guideline, and depends on how much change in practice or services is needed. Implementing change is most effective when aligned with local priorities.

Changes recommended for clinical practice that can be done quickly – like changes in prescribing practice – should be shared quickly. This is because healthcare professionals should use guidelines to guide their work – as is required by professional regulating bodies such as the General Medical and Nursing and Midwifery Councils.

Changes should be implemented as soon as possible, unless there is a good reason for not doing so (for example, if it would be better value for money if a package of recommendations were all implemented at once).

Different organisations may need different approaches to implementation, depending on their size and function. Sometimes individual practitioners may be able to respond to recommendations to improve their practice more quickly than large organisations.

Here are some pointers to help organisations put NICE guidelines into practice:

1. Raise awareness through routine communication channels, such as email or newsletters, regular meetings, internal staff briefings and other communications with all relevant partner organisations. Identify things staff can include in their own practice straight away.
2. Identify a lead with an interest in the topic to champion the guideline and motivate others to support its use and make service changes, and to find out any significant issues locally.
3. Carry out a baseline assessment against the recommendations to find out whether there are gaps in current service provision.
4. Think about what data you need to measure improvement and plan how you will collect it. You may want to work with other health and social care organisations and specialist groups to compare current practice with the recommendations. This may also help identify local issues that will slow or prevent implementation.
5. Develop an action plan, with the steps needed to put the guideline into practice, and make sure it is ready as soon as possible. Big, complex changes may take longer to implement, but some may be quick and easy to do. An action plan will help in both cases.
6. For very big changes include milestones and a business case, which will set out additional costs, savings and possible areas for disinvestment. A small project group could develop the action plan. The group might include the guideline champion, a senior organisational sponsor, staff involved in the associated services, finance and information professionals.
7. Implement the action plan with oversight from the lead and the project group. Big projects may also need project management support.
8. Review and monitor how well the guideline is being implemented through the project group. Share progress with those involved in making improvements, as well as relevant boards and local partners.

NICE provides a comprehensive programme of support and resources to maximise uptake and use of evidence and guidance. See the 'into practice pages' for more information.

Also see Leng G, Moore V, Abraham S, editors (2014) Achieving high quality care – practical experience from NICE. Chichester: Wiley.

Implementation Tools

Clinical Algorithm

Foreign Language Translations

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report

Categories

IOM Care Need

End of Life Care

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Collaborating Centre for Cancer. Non-Hodgkin's lymphoma: diagnosis and management. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jul 20. 25 p. (NICE guideline; no. 52).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Jul 20

Guideline Developer(s)

National Guideline Alliance - National Government Agency [Non-U.S.]

Source(s) of Funding

The National Collaborating Centre for Cancer (NCC-C) was commissioned by the National Institute for Health and Care Excellence (NICE) to develop this guideline.

Guideline Committee

Guideline Committee

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Committee (GC) members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, share-holdings, research funding (either in the form of programme or project grants or personal research awards), fellowships and support from the healthcare industry. At all subsequent GC meetings, members declared new, arising conflicts of interest which were always recorded (see Appendix F in the full guideline appendices [see the "Availability of Companion Documents" field]).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in eBook and ePub formats from the NICE Web site .

Availability of Companion Documents

The following are available:

- Non-Hodgkin's lymphoma: diagnosis and management. Full guideline. London (UK): National Institute for Health and Care Excellence; 2016 Jul. 182 p. (NICE guideline; no. 52). Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Non-Hodgkin's lymphoma: diagnosis and management. Appendices. London (UK): National Institute for Health and Care Excellence; 2016 Jul. (NICE guideline; no. 52). Available from the NICE Web site .
- Non-Hodgkin's lymphoma: diagnosis and management. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence; 2016 Jul. (NICE guideline; no. 52). Available from the NICE Web site .
- Non-Hodgkin's lymphoma: diagnosis and management. Resource impact statement. London (UK): National Institute for Health and Care Excellence; 2016 Jul. 1 p. (NICE guideline; no. 52). Available from the NICE Web site .
- The guidelines manual 2012. London (UK): National Institute for Health and Care Excellence (NICE); 2012 Nov. Available from the NICE Web site .
- Developing NICE guidelines: the manual. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Oct. Available from the NICE Web site .

Patient Resources

The following is available:

- Non-Hodgkin's lymphoma: diagnosis and management. Information for the public. London (UK): National Institute for Health and Care Excellence; 2016 Jul. 18 p. (NICE guideline; no. 52). Available in English and Welsh from the National Institute for Health and Care

Excellence (NICE) Web site. Also available for download in eBook and ePub formats from the NICE Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on November 16, 2016.

The National Institute for Health and Care Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their clinical guidelines with the intention of disseminating and facilitating the implementation of that guidance. NICE has not yet verified this content to confirm that it accurately reflects that original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE clinical guidelines are prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk.

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